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Dated: May 27, 2005 Signature: ____________________
(Grace E. Yu)

Docket No.: 388512010900
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Lawrence M. KAUVAR et al.

Application No.: 10/681,013

Filed: October 7, 2003

For: METHODS TO DETERMINE NUMBERS OF PARTICLES IN MULTIPLEXED ASSAYS (AS AMENDED)

Confirmation No.: 6212

Art Unit: 1641

Examiner: D. Venci

AFTER FINAL EXPEDITED PROCEDURE -- EXAMINING GROUP 1641

AMENDMENT UNDER 37 C.F.R. § 1.116

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is in response to an Office Action herein, mailed 28 March 2005, time for response to which was set to expire 28 June 2005. Claims 1-8 were considered and rejected and the rejection was made final. This response is submitted within two months of the mailing date of the final rejection, and thus expedited procedure is requested.

Careful consideration has been given to the grounds for rejection, and the following amendment and discussion are offered in response. The amendments are directly responsive to the grounds for rejection and do not change the scope of the claims. They merely clarify the claimed subject matter so that patentability over the art can properly be assessed. Reconsideration is respectfully requested.

MAY 3 1 2005

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PTO/SB/21 (09-04)
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/681,013
Filing Date	October 7, 2003
First Named Inventor	Lawrence M. KAUVAR
Art Unit	1641
Examiner Name	D. Venci
Attorney Docket Number	388512010900
Total Number of Pages in This Submission	9

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☒ Amendment/Reply (8 pages)
  - ☒ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
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- ☐ CD, Number of CD(s) ______
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) (please identify below):

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SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	MORRISON & FOERSTER LLP		
Signature	Kate H. Murashige		
Printed name	Kate H. Murashige		
Date	May 27, 2005	Reg. No.	29,959

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Dated: May 27, 2005 Signature: ______________ (Grace Yu)

CLAIM AMENDMENTS

1. (currently amended): A composition comprising a multiplicity of different labels, wherein each different label comprises a particulate support [[~~to~~]] which is coupled both

(a) to one or more first signal-generating moieties which together generate a visible [[~~hue~~]] characterizing signal that characterizes said label, and

(b) to a second signal generating moiety directly attached to said particulate support which emits the same wavelength at the same intensity from all said different labels so as to generate a clamped value signal from each said label,

wherein the wavelength of the signal generated by said second signal-generating moiety is different from the one or more wavelengths that compose the [[~~hue~~]] characterizing signal which characterizes the label and

wherein said labels further contain reagents which permit each of them to interact specifically with a desired target.

2. (currently amended): The composition of claim 1, wherein said characterizing signal generating moieties comprise at least two different signal generating entities wherein each of the entities generates a ~~signal~~ wavelength different from that generated by the other entity(s) and wherein the resulting [[~~hue~~]] signal of the labels resulting from said ~~signals~~ wavelength(s) is varied among the different labels whereby each different label is thereby characterized by a different [[~~hue~~]] characterizing signal.

3. (currently amended): A method to ~~provide a pattern~~ determine the distribution of multiple target substances in a sample which method comprises contacting ~~an environment containing the target substances and having a multiplicity of detection spaces~~ said sample with the composition of claim 1, [[~~and~~]]

~~assessing the number and hue of any particulate labels associated with each of said detection spaces~~

wherein [[~~said~~]] the number of labels at a location in the sample is assessed by measuring the intensity of the clamped value signal emitted from the second signal generating moiety ~~in said detection space~~ attached to said particulate support,

~~thus obtaining a pattern of target substances in the environment~~

and the nature of the target substance at a location in the sample is assessed by determining the characterizing signal,

whereby the distribution of targeted substances in the sample is determined.

4. (currently amended): The method of claim 3, wherein said ~~environment~~ sample is displayed on a support suitable for viewing by microscopy.

5. (currently amended): The method of claim 4, wherein the ~~environment~~ sample comprises an intracellular environment.

6. (currently amended): The method of claim 4, wherein the ~~environment~~ sample comprises neural circuitry.

7. (previously presented): The composition of claim 1, wherein said particulate supports have diameters of 20-200 nm.

8-9. (canceled)

REMARKS

Claim 1 has been amended in an attempt to clarify what applicants have stated to be the case throughout the prosecution – that the second signal generating moiety is directly attached to the particulate support and is not attached to a target to which the particulate support is directed. Further, as the Office has consistently objected to the term "hue," the term "characterizing signal" has been substituted. As explained previously, although applicants appreciate the suggestion to substitute the term "wavelength," this is somewhat misleading since the characterizing signal (formerly called hue) may contain two or three or more wavelengths. It is the composite of these wavelengths that make up the characterizing signal. This is made explicit in the claim as well.

It should be apparent that the amendments to claim 1 are simply an attempt to conform language to the characterization of the invention described both in the specification and, for example, in the Response to the previous Office action. See, for example, page 8 of the previous Response, in the paragraph bridging pages 8 and 9. Thus, the phrase "directly attached to said particulate support" conforms with what applicants have characterized as their invention. It is believed that this was the appropriate reading of claim 1 as originally proposed since the particulate support was described as "coupled" to both the first and second signal generating moieties. Accordingly, no new matter has been added and no new issues are raised.

The amendments to claim 2 simply conform the language to claim 1 as amended.

Claim 3 has been amended in what appears to be an extensive fashion, but which in fact states the same method as previously claimed but without the terminology to which the Office evidently objects. Again, no new matter has been added and no new issues are raised; the amendment to claim 3 is a good faith attempt to accommodate the wording preferences set forth by the Office.

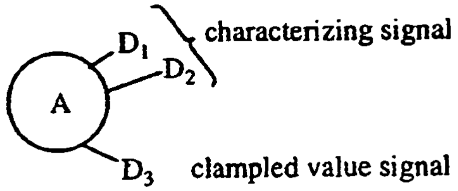
Claim 8 has been canceled to expedite prosecution.

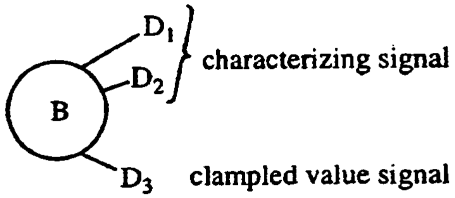
Applicants respectfully request the Office exercise its discretion and enter the amendments as proposed.

The Invention

The invention is directed to compositions of particulate labels, which particulate labels have both characterizing signals and a clamped value signal that acts as a "counter" for each label. It is possible using such compositions to determine the distribution of targets in a sample to which the labels will be bound because when the composition is applied to the sample and the particles in the composition thus distributed according to their ability to bind each target (by virtue of the reagent associated with the particulate support) each particulate support (label) bound to a target can be counted by virtue of the clamped value signal it generates and the nature of the particle can be determined by the characterizing signal it emits. The characterizing signal constitutes one or more wavelengths of emitted light. If more than one wavelength is emitted, the characterizing signal constitutes the collection of emitted wavelengths, so that the nature of the particle, and thereby the nature of the target, can be determined.

For purposes of illustration, two different particles in the composition would appear as follows:





As seen, particle A and particle B both contain the same dye in the same amount as the clamped value signal and contain the combination of D_1 and D_2 in different ratios as the characterizing signals. Clearly D_3 is directly attached to the particle in each case.

The Formal Rejections

1. Claim 3 was rejected as assertedly failing to comply with the written description requirement. The Office objects to reference to "a multiplicity of detection spaces." This phrase no longer appears, so this basis for rejection may be withdrawn.

2. Claim 1 was rejected under 35 U.S.C. § 112, paragraph 2, based on the recitation of the term "hue." This term no longer appears in claim 1, so this basis for rejection may also be withdrawn.

3. Claim 3 was rejected as indefinite by virtue of the word "pattern." Again, this term no longer appears, thus permitting the Office to withdraw this objection.

4. The rejection of claim 8 is obviated by cancellation of this claim.

The Art Rejections

Claims 1-4 and 7 were rejected as assertedly anticipated by Nie, *et al.*, U.S. 2003/0148544. It is clear from the description of the rejection, and specifically with respect to the rationale set forth on page 7 in the response by the Office to the previous arguments, that the maintenance of the rejection is based on the assumption that the claim does not make clear that the clamped value signal (*i.e.*, the second signal generating moiety) is actually coupled to this particulate support. As stated, the Examiner considers that the claim "can be much more broadly construed to include a composition comprising a second signal generating moiety wherein the second signal generating moiety may or may not be coupled to the particulate support." It has never been the intention of applicants to claim compositions wherein the second signal generating moiety may or may not be coupled to the particulate support, and the amendment to claim 1 makes this very explicit. Accordingly, in view of the amendment to claim 1, it appears that this basis for rejection may properly be withdrawn. Similar comments apply to claim 2 which depends from claim 1 and to claims 3, 4 and 7 which also depend from claim 1. As explained in the Response to the previous Office Action containing this rejection, the method of Nie does not provide such second signal generating moiety (*i.e.*, the clamped value signal) attached to the particulate support at all. Nie has an entirely different approach to sample analysis from that of the present invention.

Claims not included in the rejection for anticipation (claims 5-6) were rejected as obvious over the combination of Nie with Kauvar. It is believed that this basis for rejection may be withdrawn on the same basis as that with regard to claims 1-4 and 7. Since the compositions and methods of claims 1 and 3 are not taught by Nie, the combination with Nie with Kauvar does not suggest claims 5 and 6.

Conclusion

The claims have been amended in strict conformance to what is needed to obviate the rejections set forth by the Office. No new issues are raised. The claims are of the same scope and cover the same subject matter as those previously presented; they merely conform the language to that which is apparently required by the Office in order to make the scope clear. In view of these amendments, it is believed that all bases for rejection may be withdrawn and applicants request that claims 1-7 be passed to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 388512010900.

Respectfully submitted,

Dated: May 27, 2005

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